UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION	**MDL No. 2875**
THIS DOCUMENT RELATES TO ALL CASES	**HON. ROBERT B. KUGLER** **CIVIL NO. 19-2875 (RBK)**

PLAINTIFFS' BRIEF IN OPPOSITION TO DEFENDANTS' DAUBERT MOTION TO EXCLUDE THE LIABILITY OPINION OF PLAINTIFFS' EXPERT DR. SUSAN BAIN

MAZIE SLATER KATZ & FREEMAN, LLC
103 Eisenhower Parkway, Suite 207
Roseland, New Jersey 07068
(973) 228-9898
Attorneys for Plaintiffs

On the Brief:
Adam M. Slater, Esq.
Christopher Geddis, Esq.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Rules

Regulations

PRELIMINARY STATEMENT

Dr. Susan Bain has worked in the field of quality and current good manufacturing practices ("cGMPs") since 1988. She has conducted cGMP inspections while working at the FDA, been employed by manufacturers, and as a consultant on behalf of manufacturers, with regard to quality and cGMPs, and teaches quality and cGMPs at University of Southern California School of Pharmacy. Dr. Bain's qualifications to opine on the cGMP and the related issues addressed in her report are more than adequate, and cannot be seriously challenged.

Defendants also fail to acknowledge or contend with the fact that Dr. Bain's methodology is rooted in the methodological touchstones for cGMPs; the governing cGMP regulations and guidances, as well as the internal protocols implemented by ZHP to define its cGMP obligations pursuant to those regulations. Defendants instead resort to mischaracterizations of Dr. Bain's opinions, partial citations, and hyper-technical but inconsequential attacks on Dr. Bain's methodology.

In essence, the defense previews a cross-examination that would go to the weight of the conclusions reached, at most, but in no way do they establish that Dr. Bain lacked necessary qualifications or failed to apply an acceptable methodology. The motion should be denied.

STATEMENT OF FACTS

The NDMA and NDEA that contaminated ZHP's valsartan API were formed as a direct result of the two ZHP-created manufacturing processes at issue, the TEA with sodium nitrite quenching process, and the zinc chloride process.[1] The root cause of the formation of these

[1] The FDA has concluded that "NDMA and NDEA are probable human carcinogens and should not be present in drug products," the EPA considers NDMA and NDEA to be probable human carcinogens, and **USP has said that "their presence in medicines, even at trace level is considered unacceptable because Nitrosamine impurities are probable human carcinogens**." (FDA, *FDA presents interim limits of nitrosamines in currently marketed ARBs* (Dec. 19, 2018)

genotoxic, carcinogenic impurities is described in multiple ZHP internal documents. For example, in the email written by ZHP employee Jinsheng Lin, Ph.D. on July 27, 2017, to multiple high-level employees of ZHP, Dr. Lin (whose job was to identify impurities in ZHP drug products and their mechanism of creation) confirmed that there was NDMA in the valsartan, this was caused by the quenching of sodium azide with sodium nitrite, that this was a known problem with manufacture of sartans, and this was a serious cGMP problem. (ZHP0019057 (Ex. 26); Min Li 4/20/21 Dep. Tr. 82:11-83:7, 85:7-86:2, 86:6-14, 87:19-88:7, 88:13-90:2, 90:7-10, 90:14-23 (Ex. 35)). Later, after the impurities were discovered by ZHP API customer Novartis (in Ireland), and ZHP was forced to finally disclose this serious problem, ZHP concluded in its Deviation Investigation Reports that the root cause for the creation of the NDMA/NDEA was the sodium nitrite quenching of sodium azide—[redacted]. (PRINSTON00075810-11, 75854 (Ex. 36)).

ZHP's fanciful position is that nobody could have known about the potential presence of the amines and these well-known chemical reactions, relying largely on out of context overreading of general FDA statements about the nitrosamine contamination. With regard to the introduction of dimethylamine to the zinc chloride process, Dr. Bain testified regarding a 2001 WHO monograph that stated, "DMF sold commercially contains trace amounts of … dimethylamine." (Dr. Bain Dep. Tr. 236:15-21 (Ex. 2 to Defs.' Mot.) (quoting Long & Meek, *Concise International Chemical Assessment Document 31: N,N-Dimethylformamide* (WHO 2001) (Ex. 29))). Dr. Bain's supplemental reliance list also contains a 1977 article that agrees with the FDA's Warning Letter

(emphasis added) (Ex. 31); EPA, *N-Nitrosodimethylamine* (Ex. 32); EPA, *N-Nitrosodiethylamine* (Ex. 32); USP, Summary, Highlights and Timeline of General Chapter <1469> Nitrosamine Impurities (July 20, 2018) (Ex. 34)). Unless otherwise noted, all referenced exhibits are from Adam M. Slater's Certification in Opposition to Defendants' Daubert Motion to Exclude the Liability Opinion of Dr. Susan Bain.

that dimethylamine is the PRIMARY impurity/degradant of DMF. (Juillard, *Dimethylformamide: Purification, Tests For Purity And Physical Properties*, Int'l Union of Pure and Applied Chem (Pergamon Press 1977) (Ex. 30); PRINSTON00077339, 342 (Ex. 25)).

The FDA directly addressed the cGMP violations, the resulting adulteration of the valsartan, and ZHP's inadequate excuse for its failings, in the November 30, 2018 Warning Letter to ZHP:

> **This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).**
>
> Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, **your API are adulterated** within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).
>
> * * *
>
> In November 2011 you approved a valsartan API process change (PCRC - 11025) that included the use of the solvent DMF. Your intention was to improve the manufacturing process, increase product yield, and lower production costs. However, you failed to adequately assess the potential formation of mutagenic impurities when you implemented the new process. **Specifically, you did not consider the potential for mutagenic or other toxic impurities to form from DMF degradants, including the primary DMF degradant, dimethylamine.** According to your ongoing investigation, dimethylamine is required for the probable human carcinogen NDMA to form during the valsartan API manufacturing process. NDMA was identified in valsartan API manufactured at your facility.
>
> You also failed to evaluate the need for additional analytical methods to ensure that unanticipated impurities were appropriately detected and controlled in your valsartan API before you approved the process change. **You are responsible for developing and using suitable methods to detect impurities when developing, and making changes to, your manufacturing processes. If new or higher levels of impurities are detected, you should fully evaluate the impurities and take action to ensure the drug is safe**

> **for patients.**
>
> Your response states that predicting NDMA formation during the valsartan manufacturing process required an extra dimension over current industry practice, and that that your process development study was adequate. **We disagree. We remind you that common industry practice may not always be consistent with CGMP requirements and that you are responsible for the quality of drugs you produce.**

(PRINSTON00077339, 342 (emphasis added) (Ex. 25)).

[redacted] (ZHP00662308 (Ex. 37)). This language was removed from the final draft, but the truth remains. ZHP has stipulated that it did not consult any scientific literature regarding potential risks of use of the solvents and sodium nitrite used in the manufacturing processes. (Ex. 38).

As a result of the failure to account for the potential risks of the chemicals and reactions introduced by ZHP's changes to the manufacturing process, ZHP failed to test for the presence of nitrosamines. The technology to do so, either GC-MS (gas chromatography-mass spectrometry) or LS-MS (liquid chromatography-mass spectrometry) was readily available beginning long before the development and use of these processes, as admitted by ZHP's expert on that point, Dr, Xue. (Xue Dep. Tr. 247:20-248:11 (Ex. 39)). This was documented in the literature, for example the 1978 IARC publication *Some N-Nitroso Compounds*, states, "The principal techniques employed for the analysis of volatile *N*-nitros-amines have been described in a recent publication (Presussman, *et al.*, 1978)," and "[t]he relative merits of high- and low-resolution mass spectrometry are discussed, since use of mass spectrometry as a confirmatory technique is particularly important." (P. 40 (Ex. 28)). Another article published in 2008, titled *Identification and Control of Impurities for Drug Substance Development using LC/MS and GC/MS*, discusses

the use of GC-MS and LC-MS to identify impurities in the pharmaceutical industry. (Ex. 40). In fact, ZHP's own documents demonstrate the use by ZHP of GC-MS to evaluate ZHP manufactured drug substances, going back to at least 2009. (ZHP01746278 (Ex. 41); SYNCORES00001458 (Ex. 42); SOLCO00027588 (Ex. 43)). This technology was readily available and should have been used during the development process, and thereafter once manufacturing began for commercial sale, and this would have identified the NDMA and NDEA without difficulty. (Dr. Hecht 7/6/2021 R. 7, 20-21 (Ex. 44); Dr. Hecht 10/31/2022 R. 1, 4-6 (Ex. 45)).

We know that the presence of NDMA and NDEA would not have been difficult to identify because ZHP customer Novartis did exactly that in June 2018. (ZHP00359798 (Ex. 46)). Novartis had noted small unknown peaks on standard gas chromatography, and when ZHP failed to identify the source of those peaks, Novartis did so on its own. [redacted]. (ZHP01390018 (Ex. 47)). Novartis thus identified the NDMA with one hand tied behind its back, since Novartis did not know the full process and all substances and chemicals used in the manufacturing process. ZHP did have this information along with the entire route of synthesis ("ROS").

LEGAL ARGUMENT

I.

DR. BAIN IS QUALIFIED TO OFFER HER OPINIONS

Despite this Court's guidance that "qualifications [are] really never an issue," Defendants devote most of their brief arguing the contrary. (02/28/2022 Tr. 33:4-5). Federal Rule of Evidence 702 states that "a witness [may be] qualified as an expert by knowledge, skill, experience, training, or education." The Third Circuit has interpreted this requirement liberally:

> [U]nder Rule 702, an individual need possess no special academic credentials to serve as an expert witness....'[P]ractical experience as

> well as academic training and credentials may be the basis of qualification (as an expert witness).' " (citation omitted)). **We have interpreted the specialized knowledge requirement liberally, and have stated that this policy of liberal admissibility of expert testimony "extends to the substantive as well as the formal qualification of experts."** *See, e.g.*, *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 741 (3d Cir.1994). **However, "at a minimum, a proffered expert witness ... must possess skill or knowledge greater than the average layman...."** *Aloe Coal Co. v. Clark Equip. Co.*, 816 F.2d 110, 114 (3d Cir.1987).

Waldorf v. Shuta, 142 F.3d 601, 625 (3d Cir. 1998) (emphasis added); *see also Betterbox Comms Ltd. v. BB Techs., Inc.*, 300 F.3d 325, 327-28 (3d Cir. 2002) (same); *Int'l Mrkt. Brands v. Martin Int'l Corp.*, 882 F.Supp.2d 809, 813-14 (W.D. Pa. 2012) (same); *Smolow v. Hafer*, 513 F. Supp. 2d 418, 425-26 (E.D. Pa. 2007). Under this liberal standard, the Third Circuit has adopted a broad view, for example, in holding that a social worker could serve as a vocational expert:

> **Even if his qualifications are, as the district court described, "a little thin," he has substantially more knowledge than an average lay person regarding employment opportunities for disabled individuals. In the circumstances, we cannot say that the district court abused its discretion in determining that Rizzo possessed the minimum qualifications necessary to testify as an expert.**

Waldorf, 142 F.3d a 627 (emphasis added). Dr. Bain has "substantially more knowledge" about cGMPs than "an average lay person."

At the fundamental level, **"it is an abuse of discretion to exclude testimony simply because the trial court does not deem the proposed expert to be the best qualified or because the proposed expert does not have the specialization that the court considers most appropriate."** *Holbrook v. Lykes Bros. S.S. Co.*, 80 F.3d 777, 782 (3d. Cir. 1996) (emphasis added); *see also Pineda v. Ford Motor Co.*, 520 F.3d 237, 245 (3d Cir. 2008) (same); *Ford v. Ford Motor Co.*, 311 F. Supp. 3d 667, 674 (D.N.J. 2017) (same). Moreover, an expert may rely on other subject matter experts as long as the expert "attempt[s] to assess the validity of any of the

assumptions the other experts used to formulate their opinions," especially when the other expert is disclosed and expected to testify at trial. *In re TMI Litig.*, 193 F.3d 613, 714-16 (3d Cir. 1999).

In fact, **"most arguments about an expert's qualifications relate more to the weight to be given the expert's testimony than to its admissibility."** *In re Johnson & Johnson Talcum Powder Prod. Mktg., Sales Pracs. & Prod. Litig.*, 509 F. Supp. 3d 116, 197 (D.N.J. 2020) (emphasis added) (quoting *Holbrook*, 80 F.3d at 782). Thus, **"[i]f the expert meets liberal minimum qualifications, then the level of the expert's expertise goes to credibility and weight, not admissibility."** *Kannankeril v. Terminix Int'l, Inc.*, 128 F.3d 802, 809 (3d Cir. 1997) (emphasis added).

A. Dr. Bain has the requisite training and experience to serve as an expert in this case.

Dr. Bain is qualified to opine on ZHP's failure to comply with cGMPs in manufacturing its valsartan, and the related issues addressed in her report. Defendants seek to impose a highly specific, high bar to qualifications, and mischaracterize and minimize her qualifications (while seizing on a few stray comments during Dr. Bain's deposition) at the same time. Defendants' arguments that Dr. Bain is not the "best qualified" and "does not have the specialization" they believe to be the litmus test—direct involvement in the manufacture of API, are not in line with the legal standard. *Wolfe v. McNeil-PPC, Inc.*, 881 F.Supp.2d 650, 658 (E.D. Pa. 2012) (citing *Kannankeril v. Terminix Int'l, Inc.*, 128 F.3d 802, 809 (3d Cir. 1997)). In *Wolfe*, three challenged experts were found qualified to testify "regarding defendants' compliance with applicable FDA regulations" based on less credentials than Dr. Bain presents. The Court permitted one doctor who had worked at the FDA in drug safety to testify regarding labeling and regulatory compliance, as he had "additional experience in regulatory affairs" after he left the FDA, another who was a doctor and simply authored a relevant citizen's petition and learned the regulations at that time, and had

relevant academic experience, and a third who was a doctor and had taught about FDA regulations in general, and had studied "federal regulations" as a researcher. *Id.*

Dr. Bain received her Master of Science Degree in Regulatory Science in 2003. (Dr. Bain R., Ex. A, p. 1 (Ex. 1 to Defs.' Mot.) [hereinafter Bain CV]). Dr. Bain received a Doctorate in Regulatory Science from the University of Southern California (USC) in 2011. (Dr. Bain CV, at 1). USC explains that **"Regulatory Science relates the regulatory and legal requirements of biomedical product development to the scientific research needed to ensure the safety and efficacy of those products."** USC, *Frequently Asked Questions* (Ex. 7) (emphasis added). In its press release announcing the Doctorate program, USC stated:

> ***Recall of Heparin, a widely used blood thinner, due to contaminants in shipments from in China*** *.... Lead in paint on toys prompts massive toy recalls .... Wires used in implantable heart devices are defective and recalled by the manufacturer.*
>
> **These are just a few recent headlines that have scared consumers, creating an uncertainty in the integrity of the foods we eat, the medicines we take and the medical devices we use. In order to make products safer while following government regulations, USC announced the world's first program leading to a professional doctorate in regulatory science at the 2008 Horizons Conference of the Regulatory Affairs Professional Society in San Francisco.**

Kulka Vera, *First Regulatory Science Doctorate at USC* (Apr. 21, 2008) (emphasis added) (Ex. 1). USC's website explains that the program provides "**a mature and detailed understanding of the regulations underlying global regulatory affairs**." USC, *Doctorate of Regulatory Science (DRSc)* (Feb. 26, 2010, via https://archive.org/web/) (emphasis added) (Ex. 2).

Shortly after Dr. Bain received her Doctorate in Regulatory Science, she became a Professor of Practice at Keck Graduate Institute in 2012. (Dr. Bain CV, at 1). She was also the Program Director for Keck's Master of Science Degree in Business Science Clinical and

Regulatory Affairs. (*Id.*; Keck, *Clinical and Regulatory Affairs* (Mar. 22, 2015, via https://archive.org/web/) (Ex. 3)). Keck provides a summary of that program, including in depth training regarding the regulation of drugs, diagnostic tests, and medical devices, the "**rigorous set of criteria to ensure quality and performance requirements. These standards are imposed by federal law and overseen by the Food and Drug Administration."** Dr. Bain taught at least five different courses at Keck (Ex. 4, via https://archive.org/web/), including:

> **Introduction to US Food and Drug Law:**
>
> **This course will provide students with broad general competencies in regulatory affairs for all FDA-regulated product classes (drugs, biologics and devices) throughout the product lifecycle (pre-clinical development, clinical development and post marketing). Emphasis will be placed on regulatory interactions - submissions, other communications and inspections - for each product class and for each phase of the product lifecycle.**

Keck, *Introduction to US Food and Drug Law* (Mar. 22, 2015, via https://archive.org/web/) (emphasis added) (Ex. 5).

> **Drug and Biologics Regulations:**
>
> **This course will provide students with an in-depth understanding of relationships between scientific discovery, testing and regulatory oversight of drug and biological medical products.** . .

Keck, *Drug and Biologic Regulations* (Mar. 22, 2015, via https://archive.org/web/) (emphasis added) (Ex. 6).

> **Current Issues for FDA Regulated Products:**
>
> The highly lucrative and competitive nature of this industry requires professionals have a good working knowledge, background and understanding of FDA's most recent developments, trends and legislation affecting product development, licensing and manufacturing of current and future pharmaceutical products and devices.

Keck, *Current Issues for FDA Regulated Products* (Sept. 5, 2015, via https://archive.org/web/) (Ex. 15).

In 2017, Dr. Bain left Keck to become an Assistant Professor at USC, where she is responsible for USC's Master of Science Degree in Product Quality. (Dr. Bain Dep. Tr. 57:13-21 (Ex. 2 to Defs.' Mot.)). USC describes the program as follows:

> Professionals working in quality assurance and quality control are responsible for the testing and oversight required to ensure the safety of healthcare products. **Students learn about the regulations and guidelines that ensure the quality of drugs**, biologics and medical devices **in the US and internationally, and how to apply this knowledge in the ever-expanding field of medical product development and manufacturing. They develop an understanding of the basic principles essential for the interpretation and implementation of quality practices and quality systems.**

USC, *MS in Medical Product Quality* (emphasis added) (Ex. 8). Over the last two years, she taught at least four courses relevant to the issues here, including a "drug and biologics quality course…We teach the regulations that are – that they are required to meet in manufacturing at a broad level." (Dr. Bain Dep. Tr. 114:15-116:3). USC summarizes three of the courses as follows:

> **Quality Assurance for Drugs and Biologics:**
>
> **An essential tenet of regulatory oversight is the assurance of quality through post-marketing surveillance, internal audits and regulatory inspections. Students will learn about the regulations needed to ensure the quality of drugs** and biologics **in the US and internationally, and will gain an understanding of the principles necessary for the interpretation and implementation of a quality system.**

USC, *Course Descriptions* (emphasis added) (Ex. 10).

> **Quality Systems and Standards:**
>
> **Quality assurance is a huge part of medical product development and constitutes a science in itself. In this introductory course, we will examine the way that different**

> **countries regulate the quality of medical products, from design and development to manufacturing and distribution.** We will study the rules governing good laboratory and manufacturing practices, and explore how they mesh with ISO and European standards, CE marking and quality systems regulations. **We will look at risk analysis and documentation, and participate in a real-life audit.**

USC, *Course Descriptions* (emphasis added) (Ex. 11).

> **Validation Requirements for Medical Products:**
>
> **Regulated industries, such as medical product manufacturing, must adopt and adhere to complex compliance procedures to ensure their final product meets quality, safety and purity requirements so that it is safe for distribution and / or sale. As one of the essential pharmaceutical commercialization requirements, validation assures consistent reproduceable and repeatable results as part of the Quality Management System (QMS) for testing and manufacturing processes.**

USC, *Course Descriptions* (emphasis added) (Ex. 12); *see also* USC, *Course Descriptions: Auditing Principles* (emphasis added) (Ex. 9).

Dr. Bain has also published in this field, having co-edited *An Overview of FDA Regulated Products, From Drugs and Cosmetics to Food and Tobacco* (Elsevier 2018). She co-authored the introductory chapter of the book as well as the chapter on drugs. ScienceDirect, *An Overview of FDA Regulated Products, From Drugs and Cosmetics to Food and Tobacco* (Ex. 16). Elsevier provides this description of the book:

> An Overview of FDA Regulated Products: From Drugs and Medical Devices to Food and Tobacco provides a valuable summary of the key information to unveil the meaning of critical, and often complex, regulatory concepts. **Concise and easy to read with practical explanations, key points, summaries and case studies, this book highlights the regulatory processes involved in bringing an FDA regulated product from research and development to approval and market.** Although the primary focus will be on the US system, this book also features global perspectives where appropriate.

Elsevier, *An Overview of FDA Regulated Products, From Drugs and Cosmetics to Food and*

Tobacco (emphasis added) (Ex. 17).

Dr. Bain is also a Peer Reviewer for *Therapeutic Innovation & Regulatory Science*, which "publishes peer-reviewed original research, review articles, commentaries, and letters to the editor on medical product discovery, development, regulation, access, and policy." Springer, *Therapeutic Innovation & Regulatory Science* (Ex. 14). Among other things, the "journal focuses on" "Product Development," "Regulatory Science and Policy," and "Pharmacovigilance and Product Safety." (*Id.*).

In addition to her academic work, Dr. Bain is a regulatory consultant, through her firm InCompliance Solutions, and has consulted for human drug manufacturers. (*Id.* at 226:21-24). Her CV summarizes her services, including cGMP audits, and work with multidisciplinary teams (e.g. subject matter experts in scientific areas relevant to a regulatory question), depending on the issues involved. (*Id.* at 69:16-19; Ex. A to Dr. Bain R. 3).

Defendants seek to minimize Dr. Bain's extensive education and academic work in the quality field by ignoring it, instead focusing on minute and misleading details with reference to positions she held earlier in her career. Defendants begin with Dr. Bain's time at the FDA as a Consumer Safety Officer from early 2002 to late 2003. (Dr. Bain Dep. Tr. 14:2-4). At the FDA she performed cGMP compliance audits, primarily related to medical devices, and also veterinary drugs. (*Id.* at 14:2-4, 14:17-15:9, 113:9-19). She then worked for a defendant in this case, Watson Pharmaceuticals, a generic API manufacturer, as a quality assurance manager, and regulatory affairs manager, and at the time Watson was subject to a consent decree for GMP violations that occurred before she was employed there. (*Id.* at 17:13-19:2; Dr. Bain CV, at 4).

Defendants criticize Dr. Bain for having "very few interactions with the FDA over the last 20 years." (Defs.' Br. 5). Quantity of FDA interactions is not a requirement to be qualified. Dr.

Bain's primary roles have been mostly dedicated to internal quality activities, not regulatory affairs, the second of which is the department that communicates with the FDA on behalf of a manufacturer.

Another example of Defendants' hyper-technical, misleading attacks on Dr. Bain is their focus on Dr. Bain's failure to recall working at a firm while it received a 483 or warning letter, "despite claiming on her resume that she '[c]oordinated, prepared, and revised responses" to such letters while working at Watson." (Defs.' Br. 5-6). However, the full line from her CV states "Coordinated, prepared, and reviewed responses to **deficiency letters**." (Dr. Bain CV, at 4 (emphasis added)). Aside from the fact that this took place twenty years ago, in late 2003, the FDA primarily uses the phrase "deficiency letter" to refer to responses to applications and abbreviated applications for drug approvals, including amendments to such filings. *See* 21 C.F.R. § 314.110. Dr. Bain worked on responses to these types of letters, not 483s or Warning Letters.

Defendants also question how Dr. Bain could maintain a working knowledge and interface with the FDA for product recalls and recall releases without being "responsible for communicat[ions] with the FDA about product recalls" at Watson. (Defs.' Br. 10). As explained above, Dr. Bain's Quality Assurance role was largely internal, with Regulatory Affairs holding the "responsibility" for communicating with the FDA. Thus, Dr. Bain's CV and deposition testimony are consistent. Dr. Bain's Quality Assurance/Quality Control role at Techniclone also explains why her CV says she reported adverse events to the FDA, but she testified that she was not "responsible" for reporting adverse events to the FDA. Dr. Bain handled the internal adverse event reporting process but the ultimate "responsibility" for formally sending them to the FDA rested with Regulatory Affairs, meaning she sent the adverse events to that department, which would then draft and file the regulatory submission with the FDA. Defendants do not point out that her

work for this company included support for a recall because a product incorporated a "discrepant" raw material, and participation in an FDA inspection focused on the company's quality system. (Dr. Bain Dep. Tr., 22:1-21, 27:14-28:5).

Defendants also reach back thirty years to Dr. Bain's time at Alpha Therapeutics, which her CV says included representing the Quality Control Department "during on-site FDA, state and international inspections." Without being shown her CV, Dr. Bain testified thirty years later that she recalled an audit by "French regulatory authorities," but did not "remember if FDA came to audit us." (*Id.* a 39:1-6). Defendants then allege "Dr. Bain claims on her resume to have had numerous interactions with the FDA during her private section career," in comparison to her deposition testimony that she could only remember three calls "over the last two decades." (Defs. Br. 11). A meeting at an inspection is not a call, and she would not be expected to have calls with the FDA when working in a quality role. This minutiae is not of any substantive import.

Defendants also cite entirely inapposite cases in support of their argument. In *Ortiz c. Yale Materials Handling Corp.*, the court based its decision to preclude the proposed expert mechanical engineer from testifying to a proposed safer forklift design because he had done nothing to validate his opinion, and admitted he did not have the qualifications to do so, as he was "not a statistician, an expert in biomechanics as a science, or an expert in human factors as a science." No. CIV 03–3657FLW, 2005 WL 2044923, at *6 (D.N.J. Aug. 24, 2005). The Court did emphasize the flexibility accorded to the District Court in selecting and applying the Daubert factors, depending on the "nature of the issue, the expert's particular expertise, and the subject of his testimony." *Id.* at *4 (citations omitted).

In *Elcock v. Kmart Corp.*, the court recognized the limited qualifications of the plaintiff's vocational rehabilitation expert but nevertheless affirmed the trial court's decision that he was

qualified:

> Copemann[, a psychologist by training,] has no formal training in vocational rehabilitation and [the plaintiff] must therefore rely on Copemann's practical experience to demonstrate that **he "possessed the minimum qualifications necessary to testify as an expert."** In support of Copemann's qualifications, Elcock points to Copemann's experience in helping drug addicts return to employment and to his work with the Virgin Islands Division of Workers' Compensation. Based on this background, one can presume that Copemann has learned about the difficulties disabled individuals face in employment, and has accumulated **some experience** in evaluating whether they can return to a particular job. Nonetheless, the most fundamental problem with Copemann's experience in this area is that he seems most qualified to testify on a micro-level regarding the ability of a disabled individual to return to a specific job; he does not appear particularly qualified to testify on the macro-level regarding the number of jobs in the national or local economy that the disabled individual is able to perform.
>
> On the other hand, Copemann claims to have kept abreast of the relevant literature in his field, and to have consulted the Dictionary of Occupational Titles, a standard tool of the vocational rehabilitationist. In addition, **Copemann possesses a degree in a field tangentially related to the one about which he testified, and he has also attended conferences regarding vocational rehabilitation.** Finally, in the process of testifying as an expert in similar matters, Copemann has no doubt performed his brand of vocational rehabilitation assessments. Though his efforts in this regard are not grounded in formal training, **when taken together with his review of the literature in the field and his attendance at conferences, we must acknowledge that he has "substantially more knowledge than an average lay person regarding employment opportunities for disabled individuals."**

233 F.3d 734, 743-44 (3d Cir. 2000) (emphasis added) (footnotes omitted) (citing *Waldorf v. Shuta*, 142 F.3d 601, 627 (3d Cir. 1998)). Dr. Bain has "substantially more knowledge than an average lay person regarding" cGMPs. Another case—*D&D Associates, Inc. v. Board of Education of North Plainfield*—is equally inapposite. There, an attorney was proffered as a legal malpractice expert despite lacking "particularized knowledge in public bidding and construction law." No. Civ. A. 03–1026(MLC), 2006 WL 755984, at *5 (D.N.J. Mar. 20, 2006).

Defendants also quote and mischaracterize part of a magistrate judge's decision attached to the district court's affirmance in *Dreyer v. Ryder Automobile Carrier Group* for the proposition that "[a]n 'expert's' inability to correctly answer basic questions and explain their opinions at her deposition is a telltale sign that the witness 'is not competent to offer testimony to the jury on such matters.'" (Def.'s Br. 7-8 (quoting 367 F. Supp. 2d 413, 428 (W.D.N.Y. 2005)). In that case, "when asked to explain how he would apply the general good engineering practice design principles, [the "expert"] asserted were discussed in the textbooks he cited, to an actual product design assignment, [**the "expert"] responded that the answer was beyond the scope of the deposition**." *Dreyer*, 367 F. Supp. 2d at 428 (emphasis added). Here, Dr. Bain acknowledged that she did not focus on API at the FDA or in industry, but did not refuse to answer a cGMP related question on the grounds that it exceeded her expertise. She explained that she is qualified to assess the specifics of ZHP's quality activities based on her overall knowledge base (which includes her extensive academic background): "[M]y background and training in auditing and in the ICH and FDA guidelines … address risk assessment." (Dr. Bain Dep. Tr., 162:19-163:12). Moreover, in *Dreyer*, the district court considered the "expert's" report and … deposition testimony" in affirming the exclusion of his testimony. *Id.* at 417. Dr. Bain's report—which Defendants essentially ignore— is detailed and comprehensive.

Defendants drop a footnote to cite two more irrelevant cases on this point. The first one—*United States v, Arrow-Med Ambulance, Inc.*—discusses in dicta that as "a medical doctor, [the "expert"] is not a Medicare regulations expert." No. 17-CR-73-JMH, 2018 WL 1902682, at *4 (E.D. Ky. Apr. 20, 2018). The second case—*Mancuso v. Consolidated Edison Co. of N.Y.*—held that an internist could not provide toxicology opinions. 967 F. Supp. 1437, 1445 (S.D.N.Y. 1997). Defendants also cite a case precluding "a board-certified doctor of internal medicine with a Ph.D.

in pharmacology and a specialty in geriatric" from testifying "about the regulatory structure or duties of drug manufacturers under the monograph system" for over-the-counter drugs. *In re Tylenol (Acetaminophen) Mktg., Sales Pracs., & Prods. Liab. Litig.*, No. 2:12-cv-07263, 2016 WL 4538621, at *8 (E.D. Pa. Aug. 31, 2016). In contrast, Dr. Bain has extensive experience in the quality/cGMP field and teaches quality/cGMP at a national university.

Ghorley v. Baxter Healthcare Corp is inapposite for nearly the same reason. No. 1:17-cv-3091-TCB, 2019 WL 13240522 (N.D. Ga. Sept. 19, 2019). In that case, a medical doctor was precluded from giving expert testimony as to "(1) the regulatory adequacy of product labeling for the [medical device]; (2) compliance by Baxter with respect to the current Good Manufacturing Practices (cGMPs) and other applicable Food and Drug Administration standards regarding the [device]; (3) the regulatory adequacy of Baxter's inclusion of manufacturing and design standards relating to the depth of the sponge; and (4) the regulatory adequacy of Baxter's notification procedures to the FDA," as he was a doctor and his **sole** relevant experience was his work at the FDA regarding pharmaceuticals, but the case concerned medical devices. *Id.* at *5-6. **That proposed expert critically conceded "that he is not familiar with regulations that govern medical devices.**" *Id*. at *5. In contrast, Dr. Bain's qualifications go far beyond her work at the FDA, including industry and academic work in the relevant field, and she teaches and is quite familiar with the regulations governing drugs, which are catalogued and discussed in detail in her report.

B. Dr. Bain's Understanding of the Subject Matter is More Than Sufficient.

Defendants' attacks on Dr. Bain must be seen in the context of defense counsel Ms. Davidson's elusive questioning. Defense counsel used a total of five exhibits, peppering Dr. Bain with a disjointed flurry of questions rather than asking her direct questions about the language of

her report and the relevant documents and testimony relied on, and refused over and over to show Dr. Bain the documents related to the questions, even when asked. For example, defense counsel jumped around between ICH Q8, ICH Q9, and ICH Q3 from question to question, including when Dr. Bain asked to be shown those guidelines as she was asked about them. Where Dr. Bain asked, "Again, if you'd permit me time to pull up Q8, I could better answer your question." Ms. Davidson responded by completely changing the topic, "What is your basis for your opinion that ZHP violated ICH Q10." (158:1-161:2). This tactic permeated the questioning, railroading the witness through a labyrinth of confusing questions that were appropriately objected to. Notwithstanding, Dr. Bain's testimony demonstrates that she understands the subject matter.

Defendants disingenuously criticize Dr. Bain's testimony regarding when and how ICH guidelines become binding on a manufacturer in meeting its cGMP obligations. Dr. Bain clearly testified:

> **Guidance documents do not establish legally enforceable rights or responsibilities. However, in practice, the guidance is adopted by manufacturers and considered to be binding**. 21 CFR section 10.115(d)(2) states, "You may choose to use an approach other than the one set forth in the guidance document. However, your alternative approach must comply with the relevant statutes and regulations. FDA is willing to discuss an alternative approach with you to ensure that it complies with the relevant statutes and regulations."

(Dr. Bain Dep. Tr. 238:4-239:1). This testimony is substantively accurate and absolutely methodologically sound, as it is grounded in the plain language of the governing regulations. And ZHP agrees: [redacted] (Peng Dong 3/29/2021 Dep. Tr. 35:22-24, Ex. 48).

Defendants similarly mischaracterize Dr. Bain's testimony regarding the import of ICH Q8, which is titled: *Pharmaceutical Development*. Defendants accuse Dr. Bain of having "no

understanding of what those guidelines actually say, much less what they mean for API manufacturers such as ZHP," arguing that she is incorrect in testifying that Q8 has applicability to product development, as opposed to being limited to "the suggested contents for the 3.2.P.2 (Pharmaceuticals Development) section of a regulatory submission,' not the pharmaceutical development process itself." (Defs.' Br. 12). This is a distinction without a difference, as the regulatory submission documenting pharmaceutical development reflects what is required to be done during pharmaceutical development. For example, ICH Q8 states: "The quality target product profile forms the basis of design for the development of the product. Considerations for the quality target product profile could include … [d]rug product quality criteria (e.g., sterility, **purity**, stability and drug release) appropriate for the intended marketed product." P. 11 (emphasis added) (Ex. 49). [redacted] (Dr. Bain R. 29 (emphasis added); ZHP01862679, Ex. 18).

Defendants also blatantly mischaracterize the import and title of ICH Q9, and criticize Dr. Bain because she said ICH Q9 "address[es] "Quality systems," suggesting that Quality is only addressed by Q10. (Defs.' Br. 12-13). Defendants omit the fact that Q9 is titled **Quality Risk Management**, and that ICH Q9 states, "The importance of **quality systems** has been recognized in the pharmaceutical industry and it is evident that quality risk management is a valuable component of an effective quality system." P. 2 (Ex. 50). It also states: " ***Risk assessment*** consists

of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards (as defined below)." *Id.* at 3.

Defendants also criticize Dr. Bain for disagreeing with their completely inaccurate characterization of the requirements of ICH Q3A and the applicable FDA Guidance with regard to identification of the source of unknown peaks on chromatography. Dr. Bain accurately testified (in between distracting interruptions and while being denied the opportunity to consult and read from the source documents for the exact language) that ICH Q3 and ZHP's own internal SOP (addressing genotoxic impurities) required ZHP "to evaluate those impurities." (Dr. Bain Dep. Tr., 164:17-168:1). Defendants argue, "ICH Q3A and Attachment 1 to the FDA guidance on Q3A—both of which are listed on Dr. Bain's reliance list (see Bain Rep. at 4 & Ex. B)—expressly state that manufacturers have no obligation to identify unknown peaks below a threshold of 0.10% of the maximum daily dose of a drug." (*Id.* at 13). Defendants studiously ignore that ICH Q3A makes clear that threshold is **not applicable** to extremely toxic substances. (Defs.' Br. 13-14). ICH Q3A explicitly states (1) "For impurities known to be unusually potent or to produce toxic or unexpected pharmacological effects, the quantitation/detection limit of the analytical procedures should be commensurate with the level at which the impurities should be controlled," (2) "Lower thresholds can be appropriate if the impurity is unusually toxic," and (3) "Lower thresholds can be appropriate if the impurity is unusually toxic." P. 4, Attachment 1 & 3 (Ex. 51). The FDA's 2008 draft guideline based on ICH Q3, *Genotoxic and Carcinogenic Impurities in Drug Substances and Products: Recommended Approaches* specifically confirms that NDMA and NDEA are not subject to the thresholds, stating "**there are some compounds containing certain structural groups (aflatoxin-like-, N-nitroso-, and azoxy-structures) that have extremely high carcinogenic potency and are excluded from the threshold approach**." P. 8 (Ex. 19) (emphasis added). [redacted]

[redacted] (HUAHAI-US00007898 (Ex. 20); PRINSTON00080118 (Ex. 21); Peng Dong 3/31/2021 Dep. Tr. 292:19-293:7, Ex. 52). The FDA also rejected the threshold argument, in the Warning Letter:

> You also failed to evaluate the need for additional analytical **methods to ensure that unanticipated impurities were appropriately detected and controlled** in your valsartan API before you approved the process change. You are responsible for developing and using suitable methods to detect impurities when developing, and making changes to, your manufacturing processes. **If new or higher levels of impurities are detected, you should fully evaluate the impurities and take action to ensure the drug is safe for patients.**

(PRINSTON00077339, 342 (emphasis added) (Ex. 25)).[2]

Defendants apply the same misleading threshold argument with respect to the USP specifications. (Defs.' Br. 13-14). The USP section they cite (5.60.10) states, "Any substance known to be toxic shall not be listed under *Other Impurities*," meaning that both the ICH and USP do not apply the 0.10% limit to toxic substances such as NDMA and NDEA. USP 32 § 5.60.10 (emphasis added) (Ex. 55).[3]

Defendants also argue that Dr. Bain does not understand the applicable regulations, which they say only apply to finished dose manufacturing. (Defs.' Br. 14). This disingenuous argument is directly contradicted by their own expert Dr. Chesney, who states in his report, "There are currently no FDA regulations specifying what constitutes GMP for API," as a result "FDA has

[2] In comparison, ZHP's expert Dr. Afnan adopted ZHP's false narrative on thresholds, and this is a significant methodological flaw in his approach. (Pls.' Mot. to Preclude Afnan, Br. 17-21).

[3] Section 5.60 states, "**Nonmonograph tests and acceptance criteria suitable for detecting and controlling impurities that may result from a change in the processing methods or that may be introduced from external sources should be employed in addition to the tests provided in the individual monograph**, where the presence of the impurity is inconsistent with applicable good manufacturing practices or good pharmaceutical practices." *Id.* ZHP was thus required to identify and control the NDMA and NDEA impurities at whatever level they existed.

long recognized that the CGMP requirements in the good manufacturing practice regulations for finished pharmaceuticals (21 CFR Parts 210 and 211) are valid and applicable in concept to Active Pharmaceutical Ingredient (API) manufacturing." (Chesney R. 25 (ex. 53) (quoting Compliance Program 7356.002F, "Active Pharmaceutical Ingredient (API) Process Inspection," p. 4 (Sept. 11, 2015) (Ex. 22))). The FDA also states, "Investigators are to use the finished product regulations (21 CFR 210 and 211) as guidance…." Compliance Program 7356.002F, at 6.

Defendants also criticize Dr. Bain for testifying she did not know whether the FDA employs organic chemists, has a department of chemistry, or who reviews DMFs. (Defs.' Br. 14-15). These questions do not address her opinions about ZHP's conduct, and in fact, ZHP's plan to blame the FDA and speculate as to the FDA's undisclosed inner workings is likely to be precluded on a motion in limine.

Defendants criticize Dr. Bain on yet another irrelevant point, for saying she "would need to go back and look at the dates" to see whether "there was official regulatory action between 2010 and the time of the recall" with respect to ZHP. (Dr. Bain Dep. Tr. 173:12-16). As the Court and Defendants know, only ZHP knew of its contaminated valsartan before June 2018, and [redacted] (PRINSTON00000001, Ex. 23). The prior inspections are of no moment and will likely be excluded on a motion in limine, along with ZHP's plan to blame the FDA for not catching them earlier—what matters is that ZHP was violating cGMPs the entire time. By analogy, if a person drove 100 miles an hour but didn't get caught, the person was still speeding. The FDA even explained why it did not detect the issue on its inspections over the years, stating "this particular risk would not have been identified on an inspection." FDA, *FDA Statement on FDA's ongoing investigation into valsartan impurities and recalls and an update on FDA's current findings*, p. 4 (Aug. 30, 2018) (Ex. 24).

C. Dr. Bain is Qualified to Explain the Factual Basis for Her Opinions and Incorporate the Opinions of Other Subject Matter Experts into Her Own Opinions.

Defendants argue that "Dr. Bain lacks the experience and knowledge to opine about chemical reactions." (Defs.' Br. 16). Preliminarily, Rule 702 requires an expert to opine "based on sufficient facts." Rule 702; *Jaasma v. Shell Oil Co.*, 412 F.3d 501, 513 (3d Cir. 2005). An expert may rely on other subject matter experts as long as the expert "attempt[s] to assess the validity of any of the assumptions the other experts used to formulate their opinions," especially when the other expert is disclosed and expected to testify at trial. *In re TMI Litig.*, 193 F.3d 613, 714-16 (3d Cir. 1999). Here, Dr. Bain is relying on the reports and deposition testimony of Plaintiffs' chemistry experts Dr. Hecht and Dr. Najafi, as well as confirmatory review of ZHP's internal documents and the deposition testimony of its corporate representatives, the FDA's assessments of ZHP's manufacturing practices, and relevant scientific literature. (Dr. Bain Dep. Tr. 79:18:23, 81:16-82:12, 102:10-11, 125:9-11; Dr. Bain R., Ex. B, Dr. Bain List of Docs. Rev. (containing the exhibits to numerous depositions, including the scientific literature discussed therein) (Ex. 1 to Defs.' Mot.); Dr. Bain Suppl. List of Docs. Rev. (containing additional scientific literature as well as Dr. Hecht's 1/13/23 deposition transcript, including all exhibits) (Ex. 3 to Defs.' Mot.)). Dr. Bain explained that this is the process she follows outside of litigation:

> **In the normal course, what would happen is, I would do an assessment and if we got to a point where the organic chemist as an SME subject matter expert would need to give input, I would pull an SME in for his or her advisement.**
>
> **But I would do the overall risk assessment.**

(Dr. Bain Dep. Tr. 164:1-7 (emphasis added)). Dr. Bain did the same thing here, and this does not mean she is a "mouthpiece" for the chemists. This is exactly what ZHP's cGMP expert Dr. Chesney testified he would do as well. (Chesney Dep. Tr. 222:21-223:1 (Ex. 54)). And the same

for ZHP's other cGMP expert Dr. Afnan, who is relying on Dr. Xue for chemistry issues. (Afnan R. 55-56, 80-81 (Ex. 13 to Pls.' Mot. to Preclude Afnan)). This is normal practice.

In this connection, Defendants criticize Dr. Bain for not understanding the technical differences between the different chromatography technologies, glossing over that she did understand that it was GC-MS that was the best to identify nitrosamines. (Defs.' Br. 17-18). The key is that she understands the correct technology was available and ultimately was used to identify the contaminants. "As I understand it, GCMS is the most accepted way to find NDMA." (Dr. Bain Dep. Tr. 103:16-17). Similarly, defense counsel questioned Dr. Bain about a partial phrase in her report, "high potency genotoxic," without letting her see where the phrase (which is clearly a descriptive term) appeared in her report and what it was describing. After much back and forth, Dr. Bain correctly summarized the meaning: "A substance that could cause cancers." (*Id.* at 247:22-251:6).

Defendants actually argue that Dr. Bain's testimony should be precluded where she needed to consult her report in an effort to confirm the precise accuracy of her testimony—as if a *Daubert* factor were the ability to memorize every document reviewed. For example, while defense counsel was asking about Drug Master Files and ANDAs, she sandwiched in a technical question on the difference between ZHP's two contaminating valsartan manufacturing processes. (Defs.' Br. 17). Dr. Bain identified the key point—the quenching with sodium nitrite—and asked to review her report to reconfirm the specifics—and defense counsel completely changed the subject in response. (Dr. Bain Dep. Tr. 185:6-22). The details are in the report, and Dr. Bain is permitted to consult her report when she is questioned at trial. (Dr. Bain R. 19-20).[4]

[4] Defendants cite *Krys v. Aaron*, 113 F. Supp. 3d 181, 207 (D.N.J. 2015), and claim that Dr. Bain first discussed the potential for dimethylamine to be an impurity of DMF as purchased, at her deposition. In fact, this issue is raised in her report multiple times, for example in discussing the

Defendants also focus on Dr. Bain making an inconsequential error at one point in her deposition in discussing the IARC monograph on nitrosamines, stating at one point that it discusses DMF degrading into dimethylamine. (Defs.' Br. 21). As Defendants know, Dr. Bain accurately described the IARC monograph: "[T]he formation of NDMA has been known since 1865." (Dr. Bain Dep. Tr. 79:18-80:6). The IARC monograph states, "It has been known since 1865 that the reaction of dimethylamine hydrochloride with sodium nitrite at an acidic pH yields N-nitrosodimethylamine (Fridman et al., 1971)." IARC, *Some N-Nitrsoso Compounds* (Lyon, Fr. 1978) (Ex. 28).[5]

Defendants' skewed attacks on Dr. Bain extend to the law they cite, including *Torain v. City of Philadelphia*, Civil Action No. 14-1643, 2023 WL 174952, at *5 (E.D. Pa. Jan. 12, 2023). The expert report in that case was "a clear copy and paste from record documents (depositions, investigation reports) and [another expert's] report from a separate litigation." *Id.* at *5. Here, Dr. Bain's report discusses the facts of this case extensively, in order to explain the factual basis for her opinions, which are appropriately quoted and identified.

In *Dura Auto. Sys. of Ind., Inc.*, the expert relied on the work of other undisclosed experts. 285 F.3d 609, 612-13 (7th Cir. 2002). The court held that "there no justification for not disclosing to [the defendant] the opinions of the other experts—for [the plaintiff] should have known that [the

---

ZHP deviation investigation report ("NDMA is generated by nitrosation reaction of the simultaneously presented dimethylformamide (containing degradation product/impurity dimethylamine) and nitrous acid") and the testimony of Min Li ("in some of the TEA raw material it may contain a trace amount of, you know, dimethylamine, okay, so that's one root cause…"). (Dr. Bain R. 9, 15, 20, 30, 35, 50, 60). And she relies on Dr. Hecht who also addressed this issue. In comparison, the expert report in *Krys* "contain[ed] no reference to" the issue that was ultimately excluded. 113 F. Supp. 3d at 207.

[5] Defendants ironically characterize this statement as "unremarkable." (Defs.' Br. 21). Unfortunately, ZHP has stipulated it did no literature search, and as a result did not take this potential reaction into account when developing and utilizing its zinc chloride process.

disclosed expert's] expertise did not extend to scientific issues at once crucial to the prima facie case and likely to be contested." *Id.* at 616. That did not occur here. Defendants cite a similarly irrelevant case for the same argument. *See Mushin v. Pacific Cycle, Inc.*, Civil Action No.2010–060, 2012 WL 2062396, at *4 (D.V.I. June 8, 2012) (agreeing with the defendant's "primary challenge to Green's expert report … that '[the plaintiff's expert] opinion simply regurgitates the opinion of another individual who has not been listed as a trial expert and will not be testifying,'" but **recognizing that "an expert may rely on the opinion of another expert"** (emphasis added)).

II.

DR. BAIN'S METHODOLOGY IS RELIABLE

Dr. Bain's extensive experience and expertise in cGMPs, and application of the same governing sources of authority utilized in her professional and academic work, establishes the reliability of this methodology. *Geiss v. Target Corp.*, No. 09–2208 (RBK/KMW), 2013 WL 4675377, at *4 (D.N.J. 2013) (Ex. 13) (quoting *Elcock v. Kmart Corp.*, 233 F.3d 734, 745-47 (3d Cir. 2000)). This is especially true since, "Rule 702 has a liberal policy of admissibility." *Geiss*, 2013 WL 4675377 at *4 (citing *Pineda v. Ford Motor Co.*, 520 F.3d 237, 243 (3d Cir. 2008) (other citations omitted)). "[A]n expert should only be excluded if the flaw is large enough that the expert lacks the 'good grounds' for his or her conclusions." *In re Zoloft Prods. Liab. Litig.*, 858 F.3d 787, 792-93 (3d Cir. 2017).

The Defendants' arguments, primarily based on mischaracterizations of Dr. Bain's opinions and testimony, go to the conclusions reached and the weight to be given those conclusions, at most. However, the focus of the reliability inquiry is on the expert's principles and methodology, not on her conclusions. *Glynn v. Merck Sharp & Dohme Corp.*, Nos. 11–5304, 08–08, 2013 WL 1558690, at *2 (D.N.J. April 10, 2013) (Ex. 27) (citing *Daubert v. Merrell Dow*

Pharmaceuticals, Inc., 509 U.S. 579, 594-95 (1993)). In *Player v. Motiva Enterprises LLC*, No. Civ. 02–3216(RBK), 2006 WL 166452, at *6-7 (D.N.J. Jan. 20, 2006) (citations omitted) (Ex. 56), this Court found an expert failed to satisfy the reliability requirement, as the expert failed to consider important facts without satisfactory explanation, among other things, and held: "His method is untestable and arbitrary, without a generally accepted, established, or peer-reviewed methodology, and his evaluation was conducted without any real standards." *Id.* at *7-8. None of those criticisms apply to Dr. Bain's methodology, which applies the standards that govern the application of cGMPs. Dr. Bain has confirmed that she applied the same methodology she applies in her professional and academic work, and is rooted in the controlling regulations, guidances, and the internal SOPs implemented by ZHP. (Dr. Bain R. 2-7; Dr. Bain Dep. 237:18-238:3).

Defendants criticize Dr. Bain based on the claim that "all of the documents" she relied on were provided by Plaintiffs' counsel. (Def. Br. at 23). The question was actually limited to the "regulatory documents" and "ICH documents" listed on her reliance list. (Dr. Bain Dep. Tr. 219:15-23). Defendants do not disclose that Dr. Bain confirmed she did do independent research including on the FDA website, as well as ICH Guidelines, and FDA guidance documents. (*Id.* at 75:17-76:2). Defendants also fail to explain why it is problematic for the attorney retaining the expert to provide documents to the expert, where relevant documents had been collected and used over the course of years of discovery and months of depositions. The case cited, *Kremsky v. Kremsky*, 2017 WL 663091 (E.D. Pa. Feb. 17, 2017), is clearly distinguishable. In that case, the expert employed "[a]t best," an "as-yet unaccepted 'Fraud Triangle' to impermissibly establish [the defendant's] motive to allegedly misappropriate [the plaintiff's] funds." *Id.* at *3. Defendants also resort to criticizing Dr. Bain because Plaintiffs' counsel interposed appropriate work product objections when defense counsel repeatedly asked about the drafting of the report, but that is

clearly of no moment either.

Defendants also state that Dr. Bain did not analyze the audits performed by ZHP customers prior to 2018—audits that failed to disclose the cGMP issues and contamination of the valsartan. But they fail to point to anything in those documents that disproves the concrete facts that are actually at issue. Those audits will likely be inadmissible to prove that the cGMP violations did not occur—both as a matter of evidence rules and fact. Moreover, Dr. Bain reviewed ZHP's extensive responses to the FDA's 2018 inspection and the 2018 Warning Letter, all of which fully lay out ZHP's excuses for its cGMP violations here. (*See* Ex. B to Dr. Bain R., p. 1-7). They also criticize the fact that she did not quote the entire transcript of Eric Gu, inclusive of his self-serving statements that ZHP did everything correctly. (Defs.' Br. 23). What matters is that she reviewed the transcript, was aware of and considered all the testimony (Dr. Bain Dep. Tr. 155:4-15), and provided detailed references to his testimony. (Dr. Bain R. 26-31).

Another criticism is pulled from an isolated answer indicating that ZHP's risk assessment was not adequate—suggesting that Dr. Bain did not consider what was not done, but rather only considered the end result. (Defs.' Br. 24). Defendants fail to show the Court that Dr. Bain did evaluate the risk assessment at length in her report, including, "[o]f note, the risk assessment for this process does not evaluate the potential for the substances used in the manufacturing process to react and form nitrosamines at any time…." (Dr. Bain R. 9-13, 20-24, 26-52, 69-74). She also testified about this in her deposition. For example: "They didn't fully assess the potential reaction that led to the formation of the NDMA…They should have addressed the chemistry. If they did see unknown peaks during development, those should have been assessed as well…ZHP has an internal SOP on genotoxic impurity evaluation. That was not followed…They were to identify unknown impurities. Additionally, they didn't do an adequate job on their risk assessment to

identify the potential for NDMA to be formed….They didn't adequately assess the scientific literature that was available…When there's a process change, it has to be a full risk assessment done and this assessment should have included the analysis that would have led to the knowledge of the NDMA formation. And that was not addressed in their change request." (Dr. Bain Dep. Tr. 178:7-24, 179:22-180:16, 182:5-19). None of this is controversial, as ZHP has stipulated that it failed to review any relevant scientific literature as part of its risk assessment. (Ex. 38). As stated in Dr. Bain's report, Eric Gu admitted during his 30(b)(6) deposition that cGMPs required evaluation of all the chemical reactions in the process, including "the reaction between dimethylamine (DMA) and nitrous acid that formed NDMA." (Dr. Bain R. 28; Dr. Bain Dep. Tr. 241:11-242:3). The FDA of course agreed with this analysis in its Warning Letter. (Ex. 25).

ZHP also argues that Dr. Bain cannot offer opinions that it couches as improper legal conclusions, including her opinion that ZHP violated cGMPs, and that the product was adulterated due to the contamination. However the Court ultimately determines the motions in limine prior to trial, Dr. Bain can certainly inform the jury of her opinions as to what standards and criteria ZHP was required to meet under cGMPs, and that these requirements were not met. In the context of adulteration, aside from the FDA having already found the valsartan manufactured by ZHP was adulterated, Dr. Bain is permitted to explain to the jury the criteria to define adulteration, and that this criteria was met.[6] In short, this argument is premature and can be addressed at a later date, as this does not raise a true *Daubert* issue.

Finally, Defendants criticize Dr. Bain for reciting in detail facts that she considered and relied on in her report. If Dr. Bain's report did not contain this factual background, Defendants

[6] This argument assumes that the Court will not have already ruled as a matter of law that Defendants violated cGMPs, and that the resulting contaminated drug product was adulterated. No reasonable juror could find otherwise.

would be arguing that Dr. Bain was offering net opinions. Dr. Bain is not going to simply summarize and regurgitate facts to the jury. However, to the extent relevant to explaining her opinions, she can certainly be asked about particular facts or testimony, and to explain the significance of those facts in forming her opinions. That would never be objectionable. And the cases cited by the Defendants are not on point because they go to what an expert may testify to at trial.

CONCLUSION

For the foregoing reasons, Defendants' motion to preclude Dr. Bain's opinions should be denied.

Respectfully,

By: /s/ *Adam M. Slater*

ADAM M. SLATER
Mazie Slater Katz & Freeman, LLC
103 Eisenhower Parkway
Roseland, NJ 07068
973-228-9898
Fax: 973-228-0303
aslater@mazieslater.com

Dated: April 11, 2023

CERTIFICATE OF SERVICE

I hereby certify that on April 11, 2023, I electronically filed a partially redacted version of this brief and my supporting certification with the Clerk of the Court using CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL. In addition, I hereby certify that unredacted copies of foregoing document will be served contemporaneous to filing via email on the Court, Special Master, and the Defense Executive Committee at DECValsartan@btlaw.com, with the exception of the unredacted exhibits, which will be sent to the Court on a thumb drive via FedEx and to the Defense Executive Committee via a Dropbox link.

MAZIE SLATER KATZ & FREEMAN, LLC
Attorneys for Plaintiffs

By: /s/ Adam M. Slater

Dated: April 11, 2023